“Real World Evidence”
Nuovi target terapeutici in ematologia
8 - 9 Novembre 2018
Auditorium “Fra Agostino Daniele”
San Giovanni Rotondo

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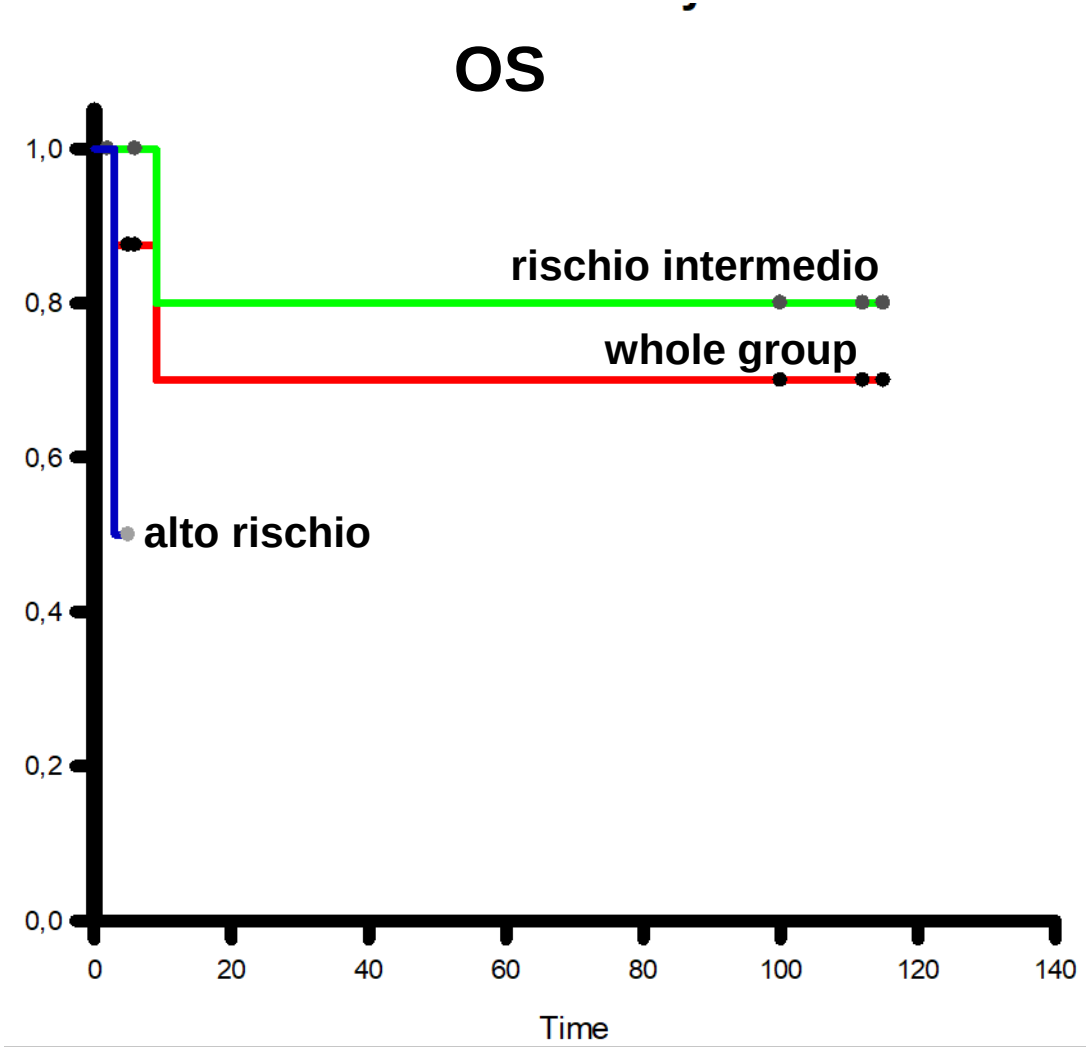
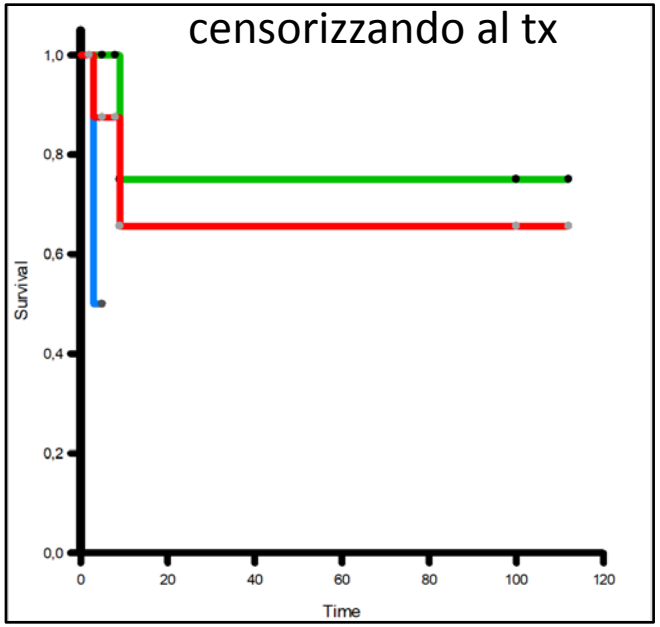
Midostaurina e LMA:
Esperienza REAL WORLD della REP

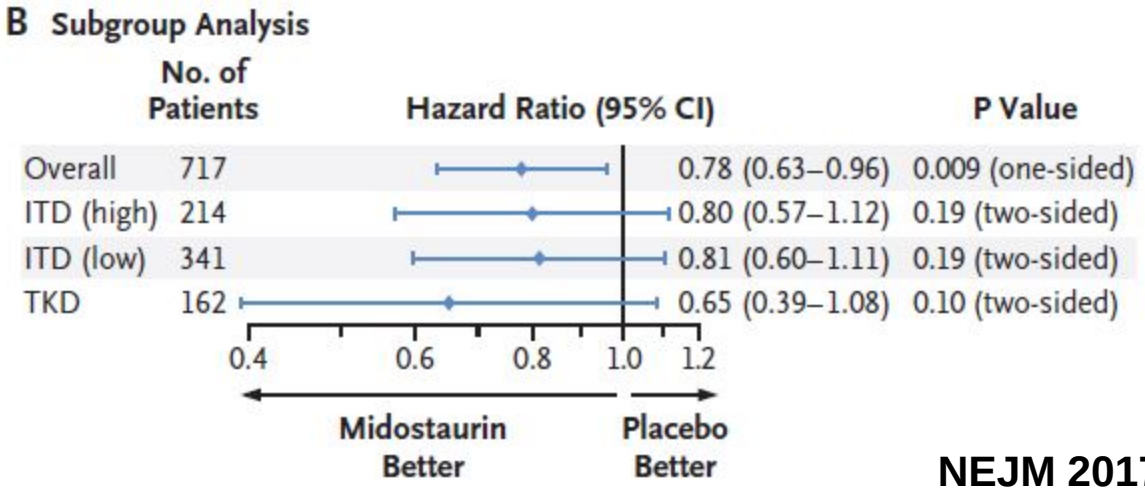
Esperienza *real world* Midostaurina - REP

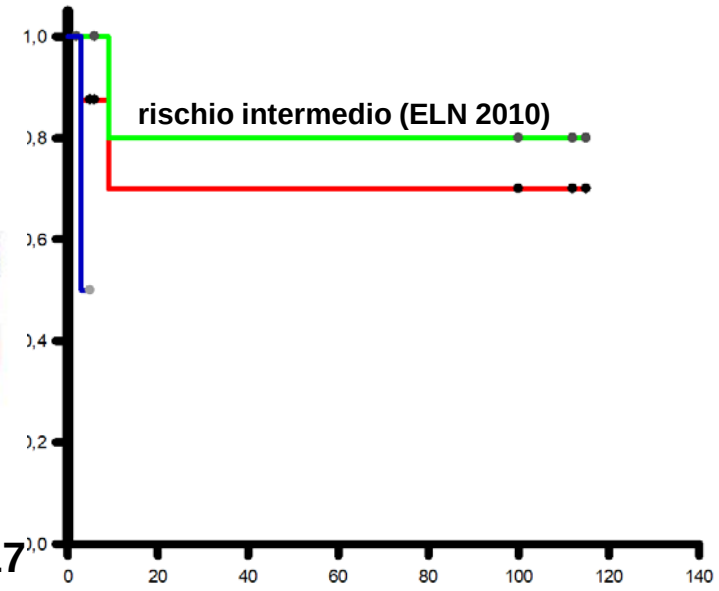
	Pz, n=9	
Età	54	
Globuli bianchi esordio	18000	
FLT3mut		
ITD	8 (89)	
D835	1 (11)	
NPMmut	3 (33)	
Citogenetica		
NK	7 (78)	
Cariotipo cx	2 (22)	
Rischio integrato genetico Molecolare		
Intermedio	7	Missing allelic ratio
Alto	2	
Fase utilizzo Mido, n (%)		
Ind	5 (56)	
Reind	1 (11)	
Consol	3 (33)	
Risposta		
CR	7 (78)	
NR	2 (22)	


OS
1,0
0,8
0,6
0,4
0,2
0,0
rischio intermedio
whole group
alto rischio
0
20
40
60
80
100
120
140
Time


censorizzando al tx
Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
20
40
60
80
100
120
Time

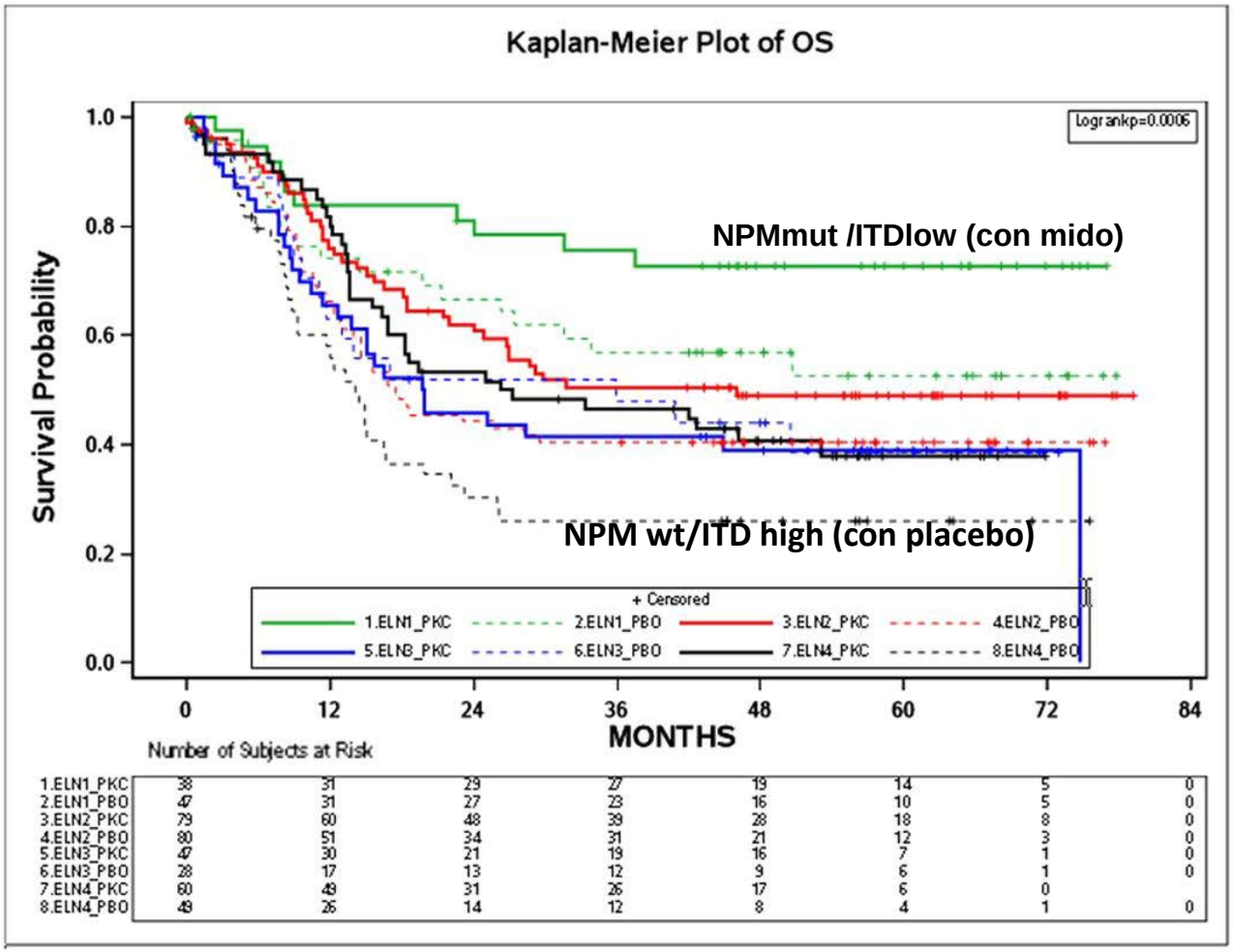
	ELN 2017-RISK in NK/ITD+
1.NPMmut low ratio	favorevole
2.NPMmut, high ratio 3.NPM wt, low ratio	intermedio
4.NPM wt, high ratio	adverse





NEJM 2017

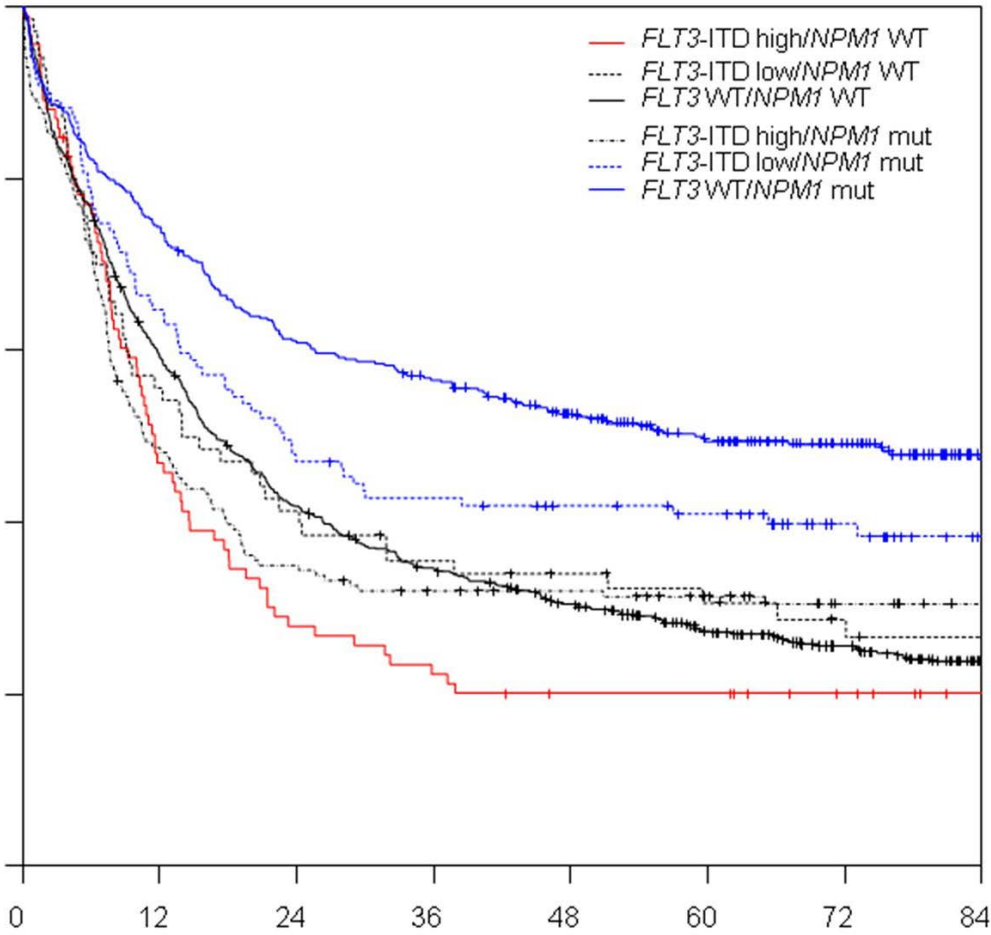
Figure 1: Overall survival for the 2017 ELN-defined *NPM1/FLT3*-ITD genotypes according to randomization: ELN1_PKC (*NPM1*^{mut}/*FLT3*-ITD^{low} M, green bold line); ELN1_PBO (*NPM1*^{mut}/*FLT3*-ITD^{low} PBO, green dashed line); ELN2_PKC (*NPM1*^{mut}/*FLT3*-ITD^{high} M, red bold line); ELN2_PBO (*NPM1*^{mut}/*FLT3*-ITD^{high} PBO, red dashed line); ELN3_PKC (*NPM1*^{wt}/*FLT3*-ITD^{low} M, blue bold line); ELN3_PBO (*NPM1*^{wt}/*FLT3*-ITD^{low} PBO, blue dashed line); ELN4_PKC (*NPM1*^{wt}/*FLT3*-ITD^{high} M, black bold line); ELN4_PBO (*NPM1*^{wt}/*FLT3*-ITD^{high} PBO, black dashed line)



Not censored at allo

Post-HOC analysis
ASH 2017;
Blood 2017; 130:417

The risk classification of the 2017 ELN recommendations according to NPM1 and FLT3-ITD genotypes was validated in this large retrospective analysis including data from 1610 patients with newly diagnosed AML with intermediate risk cytogenetic abnormalities or normal karyotype. **The time-dependent analysis of alloHCT indicated that patients with favorable AML should not receive alloHCT as post-remission therapy in CR1, whereas patients with intermediate risk or high risk AML would benefit from alloHCT in CR1.**

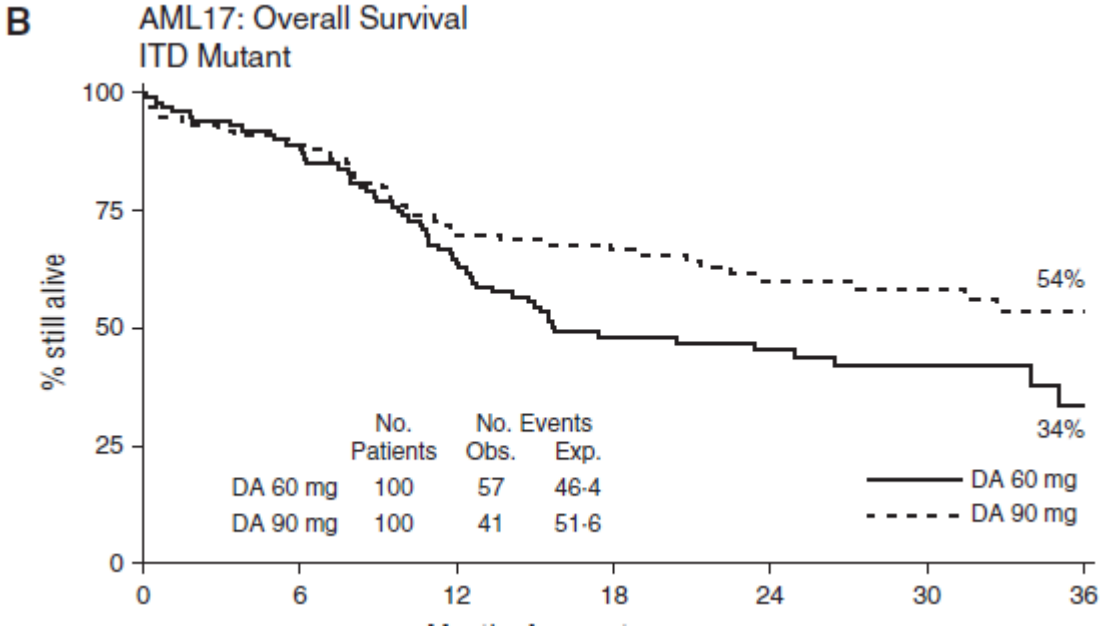


ASH 2017
Blood 2017 130:2694

Dose Dauno: 60 vs 90 mg/mq/die per 3 gg in AML ITD+

1.Luskin MR, Lee J-W, Fernandez HF, et al. Benefit of highdose daunorubicin in AML induction extends across cytogenetic and molecular groups. Blood 2016; 127: 1551-8[R].

2. Burnett AK, Russell NH, Hills RK. Higher daunorubicin exposure benefits FLT3 mutated acute mveloid leukemia. Blood 2016: 128: 449-52.



…midostaurin to conventional therapy and improved OS from 44.2%to 51.4% at 5 years, which is similar to the benefit that we show here (54%vs 34% overall at 3 years, and 53% vs 42% when censored at transplant) for the recipients of daunorubicin 90 mg/m2.

Allo tx rappresenta la migliore terapia di consolidamento in AML ITD+, con la sola eccezione …..

"…….the data indicate that only in cases in which there is an NPM1 mutation and the FLT3 mutant to FLT3 wt ratio is low does conventional chemotherapy even equal the outcomes from allogeneic transplant"

Pratz KW & Levis M
"How I treat FLT3-mutated AML"
Blood 2017

Grazie per
l’attenzione